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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/598,062	96/20/2000	Carolyn Petersen	480.75-2 (HV)	6515

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EXAMINER

GUCKER, STEPHEN

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/598,062

Applicant(s)

Petersen et al.

Examiner

Stephen Guckler

Group Art Unit

1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 2/24/03
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 19-25 & 40-49 is/are pending in the application.
- ☐ Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 19-25 & 40-49 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Other _____

Office Action Summary

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Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

3. Claims 19-24 and 40-49 are rejected under 35 U.S.C. 102(a) as being anticipated by Nesterenko et al. ("Nesterenko"). Nesterenko discloses antibodies that bind to a surface antigen proteinase of 24 kD associated with sporozoites of *Cryptosporidium parvum* from fecal specimens (abstract and page 77). This surface antigen protease was inhibited by inhibitors of both metalloproteinases and thiol proteinases, but not serine or aspartyl proteinase inhibitors (page 85). The sensitivity of the membrane-associated cysteine protease to inhibitors is similar to that of the metallo-activated cysteine proteinases calpain I and II (page 86). Therefore, the evidence seems to suggest that Nesterenko's cysteine protease is the same antigen that comprises SEQ ID NOs: 4-6 of the instant Application, and antibodies to this antigen inherently meet the limitations of the instant claims (see page 79 and page 81 also for antibody-antigen complex formations; page 78 for radioactive labeling) given the evidence at hand and absent evidence to the contrary.

Applicant's arguments filed 2/24/03 have been fully considered but they are not persuasive because Applicant argues that Nesterenko's antibodies were not associated with

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oocyst walls, rhoptries or micronemes which are internal structures and the surface localization of Nesterenko's antibodies is consistent with the Examiner's observation that Nesterenko's antibodies bound to a surface antigen protease. Applicant goes on to argue that the specification teaches in Figure 10 and on page 24, lines 1-9 of the instant specification that cryptopain (the surface antigen that the antibodies are binding to) is found internally within sporozoites which would indicate that it cannot be the external antigen that Nesterenko's antibodies are binding to. This is unpersuasive because the specification does not provide any evidence or support for the notion that cryptopain is not a surface antigen. Rather, page 24, lines 1-9 of the instant specification present several possible hypotheses for the results of Figure 10. "Results seen in Figure 10 therefore show that cryptopain is either localized at the surface of the Cryptosporidium sporozoites, is a part of the sporozoites membrane or is localized internally and is released during the invasion of the host cell" (page 24, lines 5-9). There is absolutely no evidence of record to support Applicant's assertion that the cryptopain antigen is found internally and is not a surface antigen. The evidence of record supports the view that the cryptopain antigen is either a surface antigen or, if it is not a surface antigen, it is released to the surface during the infection process. These hypotheses have been put forth to explain the binding of antibodies to the surface of the sporozoites. If cryptopain is not a surface antigen, then it must be released to the surface during the infection process to explain antibody binding to the surface. However, there is no evidence of record that this occurs; it is merely a hypothetical supposition being put forward to possibly explain the surface location of the antigen in the event

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it is not present on the surface endogenously. The simpler explanation for the experimental results of Figure 10 is, of course, to make the reasonable conclusion based on the evidence that cryptopain is a surface antigen, absent evidence to the contrary such as data explicitly showing its internal location or translocation to the surface.

Applicant also argues that Nesterenko discloses a 24 kDa proteinase while the instant invention is a 45 kDa proteinase and therefore is different. This is not persuasive because the mature form of cryptopain is a 25 kDa proteinase and it appears that it is this mature form that is being disclosed by Nesterenko (1 kDa molecular weight difference is within reasonable experimental error between two different laboratories using electrophoresis to estimate molecular weight in one instance and deducing molecular weight by amino acid number in the other instance).

Finally, Applicant argues that cryptopain is a cathepsin-like cysteine proteinase and is distinguished from the proteinase of Nesterenko which is inhibited by inhibitors of metalloproteinases and thiol proteinases. This argument is not persuasive because Applicant is attempting to confuse the issue with a semantic argument where none exists. Nesterenko's protease is a cysteine protease (page 86), just like Applicant's cryptopain. It may also be a metallo-proteinase. These are not mutually exclusive categories. See the phrase "metallo-activated cysteine proteases" in Nesterenko, page 86. Regardless of how one wishes to classify the cryptopain protease of the instant invention and the Nesterenko protease of the prior art, the same inhibitor (E-64) inhibited both proteases. Please note that the instant disclosure teaches

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that E-64 is a "highly specific inhibitor of cryptopain" (page 41, line 14). E-64 inhibited the protease of Nesterenko. By Applicant's own teachings, the Examiner has come to the reasonable conclusion that the protease of Nesterenko and Applicant's cryptopain are one and the same. Therefore, the antibodies of Nesterenko meet the limitations of the instant claims. Contrary to Applicant's assertions, the protease of Nesterenko has not been tested against diazomethane and BAFMK, so conclusory statements by Applicant such as "the similarity of the sensitivity of Nesterenko's protease to calpains even more distinguishes the current cryptopain from the protease of Nesterenko" lacks any significant factual underpinning.

4. Claims 19-22 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nesterenko in view of Ramakrishnan et al. ("US 5,817,310, "Ramakrishnan"). The teachings of Nesterenko are set forth above. Nesterenko does not teach monoclonal antibodies. Ramakrishnan does teach the advantage of monoclonal antibodies (column 9, lines 33-46; column 12, lines 1 to column 13, line 65) which can be produced from immortalized cell lines which would then allow unlimited production of antibodies. It would have been obvious to one of ordinary skill in the art at the time of the invention to make monoclonal antibodies to any pathogen in order that the supply of said antibodies would be steady and constant from an immortalized cell line.

Applicant's arguments filed 2/24/03 have been fully considered but they are not persuasive because Applicant argues the antibodies of Nesterenko do not meet the claim limitations for the reasons argued in the 102(a) rejection set forth above. The Examiner believes he has successfully responded to these arguments above and so the rejection is maintained.

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5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

May 16, 2003

Gary D. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
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